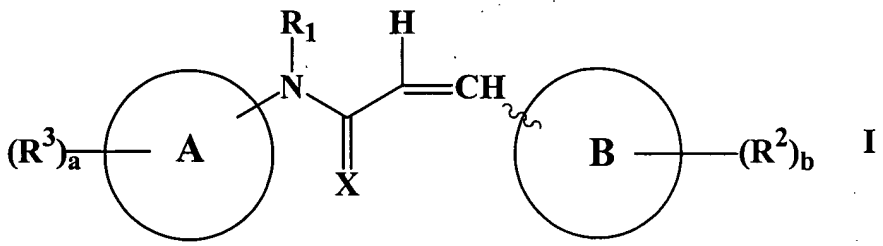
Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (previously presented) A compound of formula I:



I

wherein:

ring A and ring B are independently selected from the group consisting of aryl and heteroaryl, provided that ring A is other than pyridyl, quinazolyl or naphthyridyl;

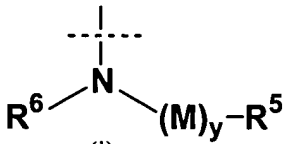
X is O or S;

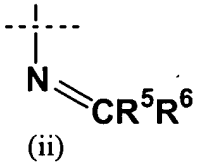
R^1 is independently selected from the group consisting of $-R^4$, $-SO_2(C_1\text{-}C_6)$alkyl, $-C(=O)R^4$, $-C(=O)OR^4$, $-C(=O)O(C_1\text{-}C_6)$alkylenearyl, $-OR^4$, $-(C_2\text{-}C_6)$alkynyl, $-(C_3\text{-}C_6)$heteroalkenyl, $-(C_2\text{-}C_6)$alkylene-OR^4, substituted aryl, unsubstituted aryl, substituted heteroaryl, unsubstituted heteroaryl, substituted aryl$(C_1\text{-}C_3)$alkyl, unsubstituted aryl$(C_1\text{-}C_3)$alkyl, substituted heteroaryl$(C_1\text{-}C_3)$alkyl and unsubstituted heteroaryl$(C_1\text{-}C_3)$alkyl;

each R^2 is independently selected from $(C_1\text{-}C_6)$alkoxy, halogen, $-C\equiv N$, $-CO_2R^4$, $-C(=O)NR^4{}_2$, $-C(=NR^4)NR^4{}_2$, $-O(C_1\text{-}C_3)$alkylene-CO_2R^4, $-(C_2\text{-}C_6)$alkylene-OR^4, phosphonato, $-NR^4{}_2$, $-NHC(=O)(C_1\text{-}C_6)$alkyl, sulfamyl, carbamyl, $-OC(=O)(C_1\text{-}C_3)$alkyl, $-O(C_2\text{-}C_6)$alkylene-$N((C_1\text{-}C_6)\text{alkyl})_2$, $-S(C_1\text{-}C_3)$alkyl, $-S(=O)(C_1\text{-}C_3)$alkyl, and $-SO_2(C_1\text{-}C_3)$alkyl;

b is 2, 3, 4, or 5;

R^3 is independently selected from halogen, $-(C_1\text{-}C_6)$alkyl, $-OR^4$, $-C\equiv N$, $-C(=NR^4)NR^4{}_2$, $-O(C_1\text{-}C_3)$alkylene-CO_2R^4, $-(C_1\text{-}C_6)$alkylene-OR^4, nitro, phosphonato, $-NHC(=O)(C_1\text{-}C_6)$alkyl, sulfamyl, $-OC(=O)(C_1\text{-}C_3)$alkyl, $-O(C_2\text{-}C_6)$alkylene-$N((C_1\text{-}C_6)\text{alkyl})_2$ and (i) and (ii) below:


(i)


(ii)

wherein:

each M is a bivalent connecting group independently selected from the group consisting of $-(C_1\text{-}C_6)$alkylene–, $-(CH_2)_d\text{-}V\text{-}(CH_2)_e-$, $-(CH_2)_f\text{-}W\text{-}(CH_2)_g-$ and –Z–;

each y is independently selected from the group consisting of 0 and 1;

each V is independently selected from the group consisting of arylene, heteroarylene, -C(=O)-, $-C(=O)(C_1\text{-}C_6)$perfluoroalkylene, –C(=O)–, –C(=S)–, –S(=O)–, $–SO_2–$, $–C(=O)NR^4–$, $–C(=S)NR^4–$ and $–SO_2NR^4–$;

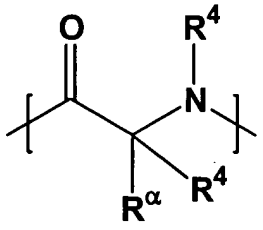
each W is independently selected from the group consisting of $–NR^4–$, –O– and -S–;

each d is independently selected from the group consisting of 0, 1 and 2;

each e is independently selected from the group consisting of 0, 1 and 2;

each f is independently selected from the group consisting of 1, 2 and 3;

each g is independently selected from the group consisting of 0, 1 and 2;

-Z- is 
;

wherein the absolute stereochemistry of –Z– is S or R, or a mixture of S and R;

each R^α is independently selected from the group consisting of -H, $-(C_1\text{-}C_6)$alkyl, $-(CH_2)_3\text{-}NH\text{-}C(NH_2)(=NH)$, $-CH_2C(=O)NH_2$, $-CH_2COOH$, $-CH_2SH$, $-(CH_2)_2C(=O)\text{-}NH_2$, $-(CH_2)_2COOH$, $-CH_2$-(2-imidazolyl), $-(CH_2)_4\text{-}NH_2$, $-(CH_2)_2\text{-}S\text{-}CH_3$, phenyl, $-CH_2$-phenyl, $-CH_2\text{-}OH$, $-CH(OH)\text{-}CH_3$, $-CH_2$-(3-indolyl), $-CH_2$-(4-hydroxyphenyl); and includes compounds wherein R^α and R^4 combine to form a 5-, 6- or 7-membered heterocyclic or carbocyclic ring;

a is 1, 2 or 3;

R^4 is independently selected from the group consisting of –H, -(C_1-C_6)alkyl, substituted -(C_1-C_6)alkyl, -(C_2-C_6)alkenyl, substituted -(C_2-C_6)alkenyl and heteroalkyl, wherein two R^4 groups may together form a heterocycle;

each R^5 is independently selected from the group consisting of -R^4, unsubstituted aryl, substituted aryl, substituted heterocyclic, unsubstituted heterocyclic, -CO_2R^4, -C(=O)NR^4_2, -C(=NH)-NR^4_2, -(C_1-C_6)perfluoroalkyl, -CF_2Cl, -P(=O)$(OR^4)_2$, -OP(=O)$(OR^4)_2$, -$CR^4R^7R^8$ and a monovalent peptidyl moiety with a molecular weight of less than 1000; provided that when y is 0 and R^5 is –CO_2R^4, then R^4 is not –H;

each R^6 is independently selected from the group consisting of –H, -(C_1-C_6)alkyl, and aryl(C_1-C_3)alkyl,

each R^7 is independently selected from the group consisting of –H, -(C_1-C_6)alkyl, –C(=O)R^8, -OR^4, -SR^4, -OC(=O)$(CH_2)_2CO_2R^6$, guanidino, NR^4_2, -$NR^4_3{}^+$, -$N^+(CH_2CH_2OR^5)_3$, halogen, phenyl, substituted phenyl, heterocyclyl, and substituted heterocyclyl; and

each R^8 is independently selected from the group consisting of R^α, halogen, -NR^4_2 and heterocycles containing two nitrogen atoms;

wherein the substituents for the substituted aryl and substituted heterocyclic groups comprising or included within R^1, R^5 and R^7 are independently selected from the group consisting of halogen, -(C_1-C_6)alkyl, -(C_1-C_6)alkoxy, -NO_2, -C≡N, -C(=O)O(C_1-C_3)alkyl, -OR^4, -(C_2-C_6)alkylene-OR^4, phosphonato, -NR^4_2, -NHC(=O)(C_1-C_6)alkyl, sulfamyl, carbamyl, -OC(=O)(C_1-C_3)alkyl, -O(C_2-C_6)alkylene-N((C_1-C_6)alkyl)$_2$ and -(C_1-C_3)perfluoroalkyl;

∿∿∿ indicates a single bond, whereby the compounds of formula I may be in either the E or the Z conformation;

provided that:

when A is phenyl, R^3 is other than 3,4,5-tri-OR^4;

when R^2 is 4-methoxy, R^3 is other than 4-methoxy;

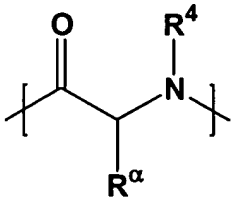
when B is phenyl, R^2 is other than 2,3-dialkoxy and 3,4-dialkoxy; and

when R^3 is halogen, R^2 is not chlorine, bromine or iodine;

or a salt of such a compound.

2. (previously presented) A compound according to claim 1,

wherein –Z– is:



;

wherein the absolute stereochemistry of –Z– is either S or R; and

each R^{α} is independently selected from the group consisting of -H, $-CH_3$, $-(CH_2)_3-NH-C(NH_2)(=NH)$, $-CH_2C(=O)NH_2$, $-CH_2COOH$, $-CH_2SH$, $-(CH_2)_2C(=O)-NH_2$, $-(CH_2)_2COOH$, $-CH_2$-(2-imidazolyl), $-CH(CH_3)-CH_2CH_3$, $-CH_2CH(CH_3)_2$, $-(CH_2)_4-NH_2$, $-(CH_2)_2-S-CH_3$, phenyl, CH_2-phenyl, $-CH_2-OH$, $-CH(OH)-CH_3$, $-CH_2$-(3-indolyl), $-CH_2$-(4-hydroxyphenyl), $-CH(CH_3)_2$ and $-CH_2CH_3$; and includes compounds wherein R^{α} and R^4 combine to form a 5-, 6- or 7-membered heterocyclic ring;

each V is independently selected from the group consisting of –C(=O)–, –C(=S)–, –S(=O)–, $-SO_2-$, $-C(=O)NR^4-$, $-C(=S)NR^4-$ and $-SO_2NR^4-$;

R^2 is independently selected from $-(C_1-C_6)$alkoxy, -C≡N, $-CO_2R^4$, $-C(=O)NR^4{}_2$, $-C(=NR^4)NR^4{}_2$, $-O(C_1-C_3)$alkylene-CO_2R^4, $-(C_2-C_6)$alkylene-OR^4, phosphonato, $-NR^4{}_2$, $-NHC(=O)(C_1-C_6)$alkyl, sulfamyl, carbamyl, $-OC(=O)(C_1-C_3)$alkyl, $-O(C_2-C_6)$alkylene-$N((C_1-C_6)alkyl)_2$, $-S(C_1-C_3)$alkyl, $-S(=O)(C_1-C_3)$alkyl, and $-SO_2(C_1-C_3)$alkyl;

b is 2 or 3;

each R^5 is independently selected from the group consisting of $-R^4$, unsubstituted aryl, substituted aryl, substituted heterocyclic, unsubstituted heterocyclic, $-CO_2R^4$, $-C(=O)NR^4{}_2$, $-C(=NH)-NR^4{}_2$, and a monovalent peptidyl moiety with a molecular weight of less than 1000; provided that when y is 0 and R^5 is $-CO_2R^4$, then R^4 is not –H; and

each R^7 is independently selected from the group consisting of –H, $-(C_1-C_6)$alkyl and $-(C_1-C_6)$acyl;

wherein the substituents for the substituted aryl and substituted heterocyclic groups comprising or included within R^1 and R^5 are independently selected from the

group consisting of halogen, -(C_1-C_6)alkyl, -(C_1-C_6)alkoxy, $-NO_2$, -C≡N, -C(=O)O(C_1-C_3)alkyl, $-OR^4$, -(C_2-C_6)alkylene-OR^4, phosphonato, $-NR^4{}_2$, -NHC(=O)(C_1-C_6)alkyl, sulfamyl, carbamyl, -OC(=O)(C_1-C_3)alkyl, -O(C_2-C_6)alkylene-N((C_1-C_6)alkyl)$_2$ and -(C_1-C_3)perfluoroalkyl; or a salt of such a compound.

3-7. (cancelled)

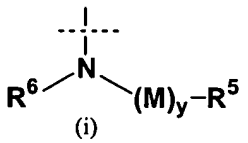
8. (withdrawn - currently amended) A compound according to claim 90, wherein:

one R^3 substituent, designated R^{3p}, is positioned in a substitution orientation relative to the -N(R^1)-C(=X)-CH=CH-(B)-R^2 moiety of Formula I which is closest to the planar angle formed by a para substituent in a six-membered aromatic ring and forms a planar angle with the -N(R^1)-C(=X)-CH=CH-(B)-R^2 moiety of between about 135° and about 180°; and

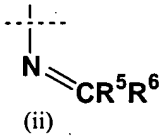
at least one R^3 substituent, designated R^{3m} is positioned in a substitution orientation relative to the -N(R^1)-C(=X)-CH=CH-(B)-R^2 moiety of Formula I which is closest to the planar angle formed by a meta substituent in a 6-membered aromatic ring and forms a planar angle with the -N(R^1)-C(=X)-CH=CH-(B)-R^2 moiety of between about 90° and about 145°;

wherein:

each R^{3m} is selected from the group consisting of -OR^4, nitro and (i) and (ii) below:



(i)



(ii)

R^{3p} is selected from the group consisting of halogen, -(C_1-C_6)alkyl, -(C_1-C_6)alkoxy, -C≡N, -C(=O)$NR^4{}_2$, -C(=NR^4)$NR^4{}_2$, –O(C_1-C_3)alkylene-CO_2R^4, $-OR^4$, -(C_2-C_6)alkylene-OR^4, phosphonato, $-NR^4{}_2$, -NHC(=O)(C_1-C_6)alkyl, sulfamyl, -OC(=O)(C_1-C_3)alkyl, -O(C_2-C_6)alkylene-N((C_1-C_6)alkyl)$_2$ and -(C_1-C_3)perfluoroalkyl;

wherein ring A, ring B, X, M, d, e, f, g, V, W, Z, R^1, R^2, R^4, R^5, R^6, R^7, a, b, y, R^α, ~~~ and any remaining R^3 substituents are as defined in claim 90; or a salt of such a compound.

9-10. (cancelled)

11. (withdrawn) A compound according to Claim 8 wherein:

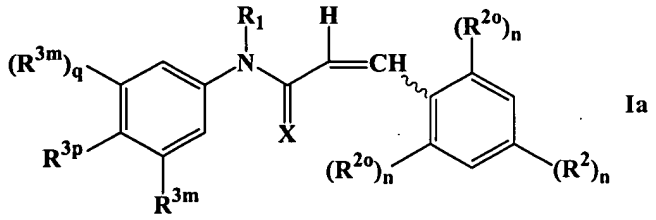
ring A is phenyl;

ring B is phenyl;

at least one R^2 substituent, designated R^{2o} is positioned at an ortho- or 1,2-substitution orientation on ring B relative to the ~CH=CH-C(=X)-N(R^1)-(A)-$(R^3)_a$ moiety of formula I; and X, M, d, e, f, g, V, W, Z, R^1, R^2, R^3, R^{3m}, R^{3p}, R^4, R^5, R^6, R^7, a, b, y, ~~~ and R^α are as defined in claim 8; or a salt of such a compound.

12-14. (cancelled)

15. (withdrawn - currently amended) A compound according to claim 11 of formula Ia:



Ia

wherein:

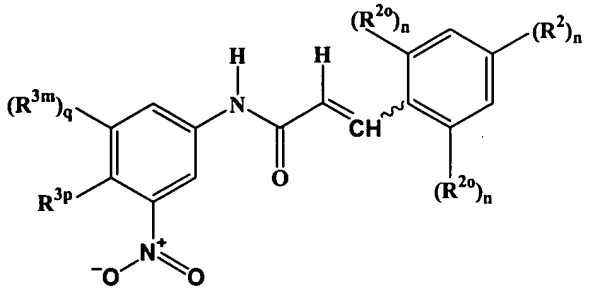
q is 0 or 1

each n is independently selected from 0 and 1; with the proviso that the sum of the values of n is selected from 2 and 3; and

~~~, X, R^1, R^2, R^{2o}, R^{3m}, and R^{3p} ~~, and n~~ are as defined in claim 11;

or a salt of such a compound.
~~~

16. (withdrawn) A compound according to claim 15 of formula Ie



Ie

wherein:

q, n, R^2, R^{2o}, R^{3m} and R^{3p} are defined as in claim 15;

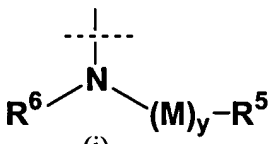
or a salt of such a compound.

17. (cancelled)

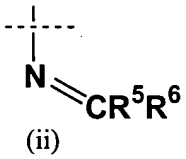
18. (withdrawn) A compound according to claim 15

wherein:

each R^{3m} is independently selected from the group consisting of (i) and (ii) below:



(i)



(ii)

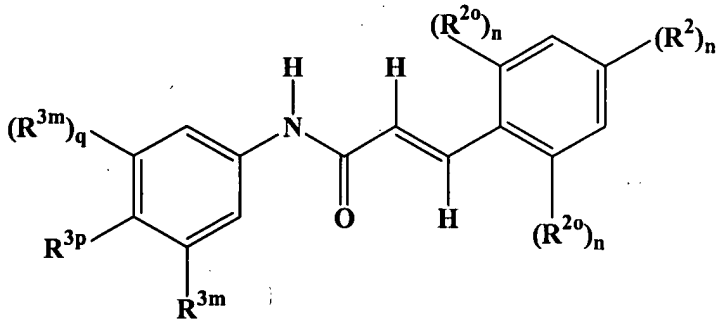
R^{3p} is selected from the group consisting of halogen, -(C_1-C_6)alkyl, -(C_1-C_6)alkoxy, -C≡N, -C(=O)NR^4_2, -C(=NR^4)NR^4_2, –O(C_1-C_3)alkylene-CO_2R^4, -OR^4, -(C_2-C_6)alkylene-OR^4, phosphonato, -NR^4_2, -NHC(=O)(C_1-C_6)alkyl, sulfamyl, -OC(=O)(C_1-C_3)alkyl, -O(C_2-C_6)alkylene-N((C_1-C_6)alkyl)$_2$ and -(C_1-C_3)perfluoroalkyl;

each R^{2o} is independently selected from the group consisting of -(C_1-C_6)alkoxy, -NR^4_2, -OC(=O)(C_1-C_3)alkyl and -O(C_2-C_6)alkylene-N((C_1-C_6)alkyl)$_2$;

R^2 is selected from the group consisting of halogen, -(C_1-C_6)alkyl, -(C_1-C_6)alkoxy, -NR^4_2, -C≡N, -CO_2R^4, -C(=O)NR^4_2, -C(=NR^4)NR^4_2, and -(C_1-C_3)perfluoroalkyl; and

X, M, d, e, f, g, V, W, Z, R^1, R^3, R^4, R^5, R^6, R^7, a, b, n, y and R^α are as defined in claim 15; or a salt of such a compound.

19. (withdrawn) A compound according to claim 18 of formula Ib



Ib

wherein:

R^{2o} is -(C_1-C_6)alkoxy;

R^2 is selected from the group consisting of halogen, -(C_1-C_6)alkyl, -(C_1-C_6)alkoxy and $-NR^4_2$;

q is 0 or 1; and

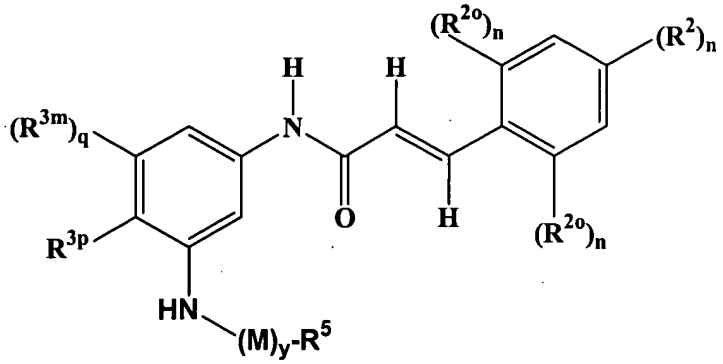
the conformation of the olefin double bond is *E*;

n, R^{3m} and R^{3p} are defined as in claim 18;

or a salt of such a compound.

20. (cancelled)

21. (withdrawn) A compound according to claim 19 of the formula Ic:



Ic

wherein R^2, R^{2o}, R^{3m}, R^{3p}, q, n, M, y and R^5 are as defined in claim 19;

or a salt of such a compound.

22. (currently amended) A compound according to claim 1, wherein the compound is selected from the group consisting of:

~~(*E*)-*N*-(4-methoxy-3-nitrophenyl)-3-(3,4,5-trimethoxyphenyl)-2-propenamide;~~

~~(*E*)-*N*-(4-methoxy-3-aminophenyl)-3-(3,4,5-trimethoxyphenyl)-2-propenamide;~~

~~(*E*)-*N*-(4-methoxy-3-nitrophenyl)-3-(2,3,4,5,6-pentafluorophenyl)-2-propenamide;~~

(*E*)-*N*-(4-bromophenyl)-3-(3-methoxy-4-fluorophenyl)-2-propenamide;

(*E*)-*N*-(4-bromophenyl)-3-(3-cyano-4-fluorophenyl)-2-propenamide;

(*E*)-*N*-(4-bromophenyl)-3-(3-carboxy-4-fluorophenyl)-2-propenamide;

~~(*E*)-*N*-(4-methoxy-3-nitrophenyl)-3-(3-fluoro-4-nitrophenyl)-2-propenamide;~~

(*E*)-*N*-(4-bromophenyl)-3-(2,4-difluorophenyl)-2-propenamide;

~~(*E*)-*N*-(4-methoxy-3-aminophenyl)-3-(3-fluoro-4-aminophenyl)-2-propenamide;~~

(*E*)-*N*-(4-methoxyphenyl)-3-(2,4,6-trimethoxyphenyl)-2-propenamide;

(*E*)-*N*-(4-methoxyphenyl)-3-(2,6-dimethoxyphenyl)-2-propenamide;

~~(*E*)-*N*-(3-hydroxy-4-methoxyphenyl)-3-(2,4,6-trimethoxyphenyl)-2-propenamide;~~

~~(*E*)-*N*-(4-methoxy-3-nitrophenyl)-3-(2,4,6-trimethoxyphenyl)-2-propenamide;~~

~~(*E*)-*N*-(4-methoxy-3-aminophenyl)-3-(2,4,6-trimethoxyphenyl)-2-propenamide;~~

2-[({5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}amino)sulfonyl]-acetic acid;

2-(*N*-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxy-phenyl}carbamoyl)acetic acid;

(2E)-*N*-[3-(amidinoamino)-4-methoxyphenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

~~2-({5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}amino)acetic acid;~~

(2E)-*N*-{3-[(3,5-dinitrophenyl)carbonylamino]-4-methoxyphenyl}-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-{3-[(3,5-diaminophenyl)carbonylamino]-4-methoxyphenyl}-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-[3-(2-chloroacetylamino)-4-methoxyphenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-{4-methoxy-3-[2-(4-methylpiperazinyl)acetylamino]-phenyl}-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-[4-methoxy-3-(phenylcarbonylamino)phenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-{4-methoxy-3-[(4-nitrophenyl)carbonylamino]phenyl}-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-{3-[(4-aminophenyl)carbonylamino]-4-methoxyphenyl}-3-(2,4,6-tri-methoxyphenyl)prop-2-enamide;

(2E)-*N*-{3-[(1Z)-1-aza-2-(4-nitrophenyl)vinyl]-4-methoxyphenyl}-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-[3-((2R)-2,6-diaminohexanoylamino)-4-methoxyphenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-[3-((2R)-2-amino-3-hydroxypropanoylamino)-4-methoxyphenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-[3-((2S)-2-amino-3-hydroxypropanoylamino)-4-methoxy-phenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-[3-(aminocarbonylamino)-4-methoxyphenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-[4-methoxy-3-(methylamino)phenyl]-3-(2,4,6-trimethoxy-phenyl)prop-2-enamide;

(2E)-*N*-[3-(acetylamino)-4-methoxyphenyl]-3-(2,4,6-trimethoxy-phenyl)prop-2-enamide;

(2E)-*N*-(3-{[(2,4-dinitrophenyl)sulfonyl]amino}-4-methoxyphenyl)-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-(3-{[(2,4-diaminophenyl)sulfonyl]amino}-4-methoxy-phenyl)-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-{3-[2-(dimethylamino)acetylamino]-4-methoxyphenyl}-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

~~2-({5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}amino)propanoic acid;~~

(2E)-*N*-(4-methoxy-3-{[4-(4-methylpiperazinyl)phenyl]-carbonyl-amino}phenyl)-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-[3-(2-hydroxyacetylamino)-4-methoxyphenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-[4-methoxy-3-(2-pyridylacetylamino)phenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(*N*-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}carbamoyl)methyl acetate;

(2E)-*N*-[3-(2-hydroxypropanoylamino)-4-methoxyphenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-{4-methoxy-3-[2-(triethylammonium)acetylamino]-phenyl}-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-(4-methoxy-3-{2-[tris(2-hydroxyethyl)ammonium]-acetylamino}phenyl)-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-[3-(2-hydroxy-2-methylpropanoylamino)-4-methoxyphenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

1-(*N*-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}carbamoyl)-isopropyl acetate;

~~(2E)-*N*-[4-methoxy-3-(2,2,2-trifluoroacetylamino)phenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;~~

(2E)-*N*-(4-methoxy-3-{[(trifluoromethyl)sulfonyl]-amino}phenyl)-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

3-(*N*-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}-carbamoyl)propanoic acid;

~~3-(*N*-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}carbamoyl)propanoyl chloride;~~

3-{[(*N*-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}carbamoyl)methyl]oxycarbonyl}propanoic acid;

4-(*N*-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}carbamoyl)butanoic acid;

(2E)-*N*-{4-methoxy-3-[2-(phosphonooxy)acetylamino]phenyl}-3-(2,4,6-trimethoxyphenyl)prop-2-enamide, disodium salt;

~~4-({5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}amino)butanoic acid;~~

~~3-({5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}amino)propanoic acid;~~

(2E)-*N*-[4-methoxy-3-(methoxycarbonylamino)phenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(2E)-*N*-(4-methoxy-3-{[(4-methoxyphenyl)sulfonyl]-amino}phenyl)-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

(*N*-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}carbamoyl)ethyl acetate;

methyl 3-(*N*-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}-carbamoyl)propanoate;

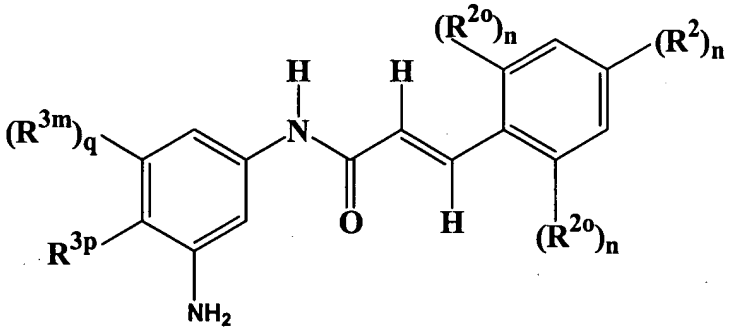
ethyl 2-(*N*-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}carbamoyl)acetate;

(2E)-*N*-[4-methoxy-3-(2,2,3,3,3-pentafluoropropanoylamino)-phenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;

methyl 2-(*N*-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoyl-amino]-2-

methoxyphenyl}carbamoyl)-2,2-difluoroacetate;
3-(*N*-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}carbamoyl)-2,2,3,3-tetrafluoropropanoic acid;
(2E)-*N*-[3-(2-aminoacetylamino)-4-methoxyphenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;
2-(*N*-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}carbamoyl)-2,2-difluoroacetic acid;
(2E)-*N*-{3-[2-(dimethylamino)-2,2-difluoroacetylamino]-4-methoxyphenyl}-3-(2,4,6-trimethoxyphenyl)prop-2-enamide;
and salts of such compounds.

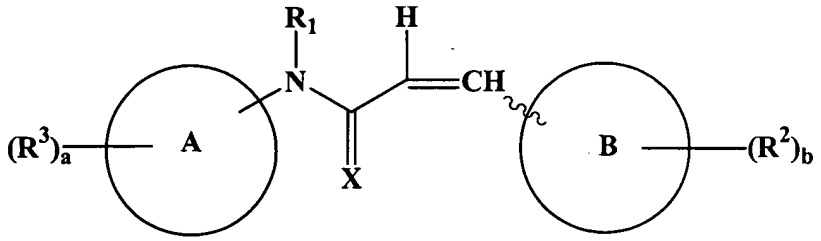
23. (withdrawn) A compound according to claim 21 of the formula Id:



Id

wherein R^2, R^{2o}, R^{3m}, R^{3p}, n, and q are defined as in claim 21, or a salt of such a compound.

24. (previously presented) A process for preparing a compound according to claim 2, which compound has the formula I,



I

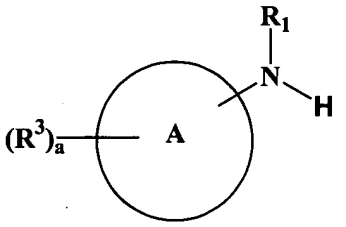
wherein:

the olefin double bond is in the *E* conformation; and

R^1, R^2, R^3, a, b, X, A and B are as defined in claim 2;

comprising:

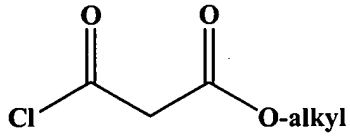
(1) coupling a compound of formula II:



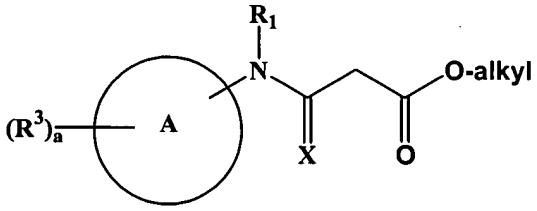
II

wherein A, R^1, R^3, and a are defined as in claim 2;

with an alkyl ester of malonic acid chloride:

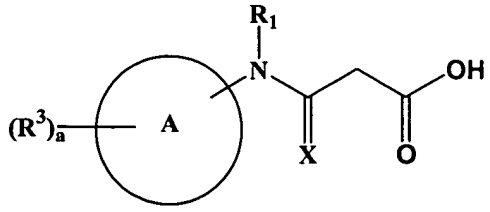


to yield a carboxylic ester compound of formula III:



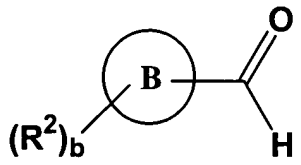
III

(2) hydrolyzing the carboxylic ester compound of formula III to form a carboxylic acid compound of formula IV:



IV

(3) coupling of the carboxylic acid compound of formula IV with an aromatic aldehyde of formula V:



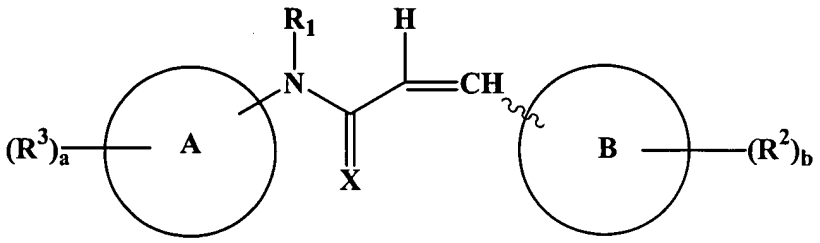
V

wherein R^2, B and b are defined as in claim 2;

in glacial acetic acid at elevated temperature to form a compound of formula I;

or a salt of such a compound.

25. (previously presented) A process for preparing a compound according to claim 2, which compound has the formula I,



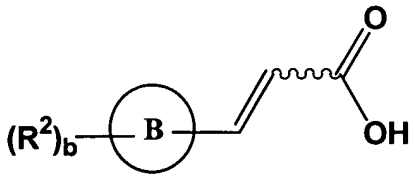
I

wherein:

R^1, R^2, R^3, a, b, X, A and B are as defined in claim 2;

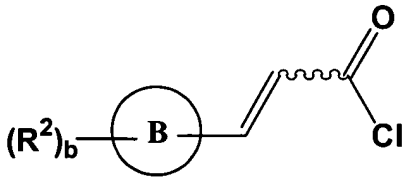
comprising:

(1) halogenating a carboxylic acid of formula VI with a halogenating agent:



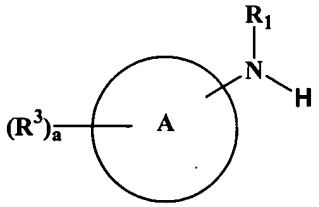
VI

to form an acid halide of formula VII:



VII

(2) coupling the acid halide VII to an aromatic amino compound of formula II

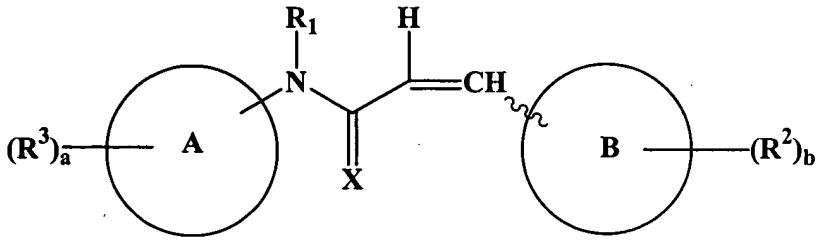


II

to form an amide compound of formula I;

or a salt of such a compound.

26. (withdrawn) A process for preparing a compound according to claim 2, which compound has the formula I,



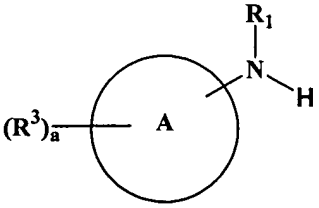
I

wherein:

R^1, R^2, R^3, a, b, X, A and B are as defined in claim 2;

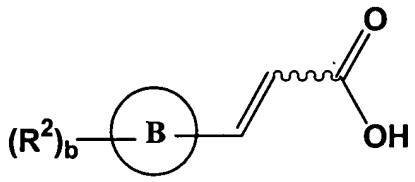
comprising:

reacting an aromatic amino compound of formula II



II

with a carboxylic acid compound of formula VI:

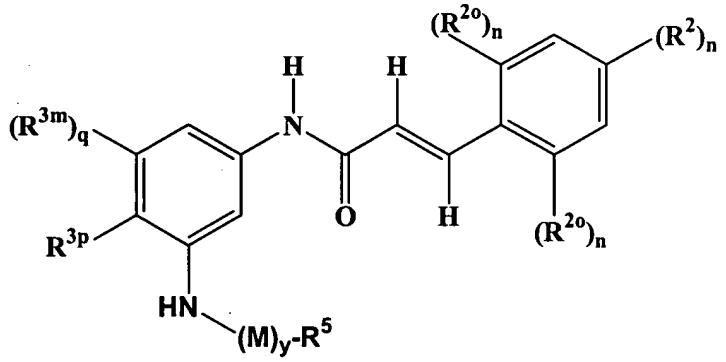


VI

and an amide coupling agent, to form a compound of formula I;

or a salt of such a compound.

27. (withdrawn - currently amended) A process for preparing a compound according to claim 21, which compound has the formula Ic:



Ic

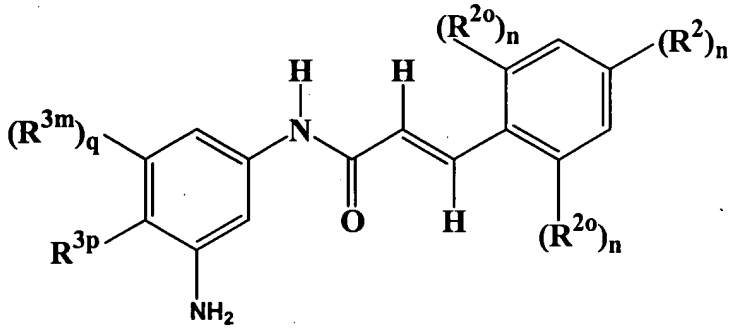
wherein:

q is 0 or 1; and

R^2, R^{2o}, R^{3m}, R^{3p}, n, M, y and ~~R^6~~ R^5 are defined as in claim 21;

comprising:

reacting an aromatic amino compound of formula Id



Id

with an electrophilic compound of formula VIII:

$$R^5—L \qquad \text{VIII}$$

wherein ~~R^5~~ L comprises an electrophilic reactive center selected from the group consisting of:

(a) an alkyl moiety having a leaving group;

(b) an aryl or heteroaryl halide or aryl or heteroaryl pseudo halide;

(c) a carboxylic acid activated with a leaving group;

(d) a sulfonic acid activated with a leaving group;

(e) a carbamic acid moiety activated with a leaving group;

(f) a cyanate moiety;

(g) an aldehyde or ketone moiety, or a hydrate thereof or a ketal or acetal thereof;

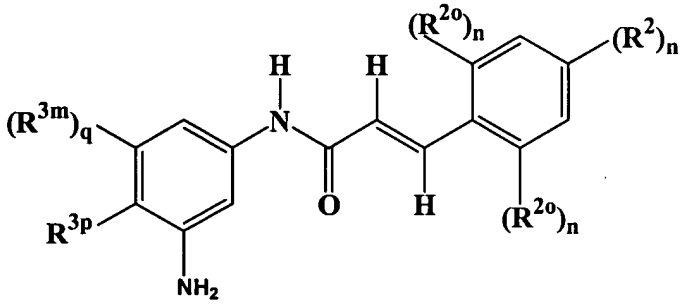
(h) a carboxylic acid moiety and an amide coupling reagent; or

(i) the intermediate product of a thiourea moiety and 2-chloro-1-methyl pyridinium iodide;

to form a compound of formula Ic,

or a salt of such a compound.

28. (withdrawn) A process for preparing a compound according to claim 23, which compound has the formula Id:



Id

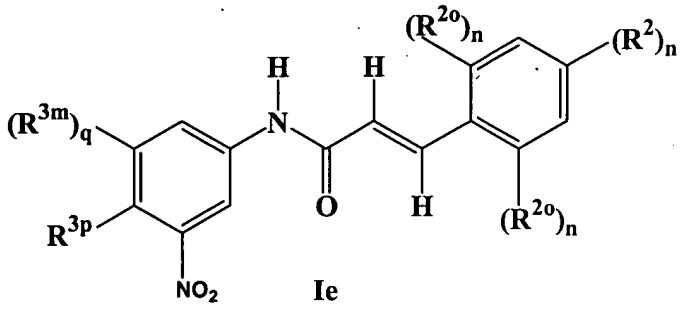
wherein:

q is 0 or 1; and

R^2, R^{2o}, R^{3m}, R^{3p} and n are defined as in claim 23;

comprising:

chemically reducing a compound of formula Ie:

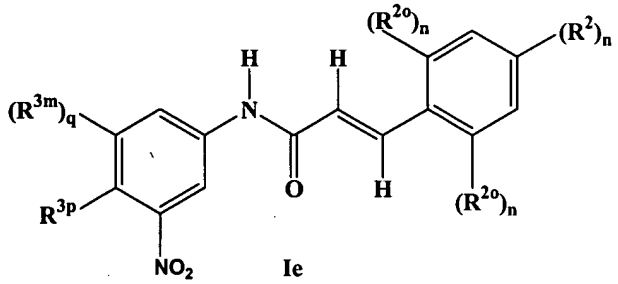


Ie

to form a compound of formula Id,

or a salt of such a compound.

29. (withdrawn) A process for preparing a compound according to claim 16, which compound has the formula Ie:



Ie

wherein:

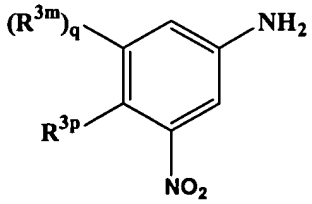
q is 0 or 1; and

R^2, R^{2o}, R^{3m}, R^{3p} and n are defined as in claim 16; and

the olefin double bond is in the *E* conformation;

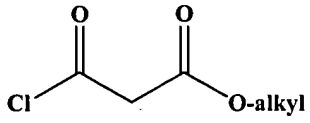
comprising:

(1) coupling a compound of formula IIb:

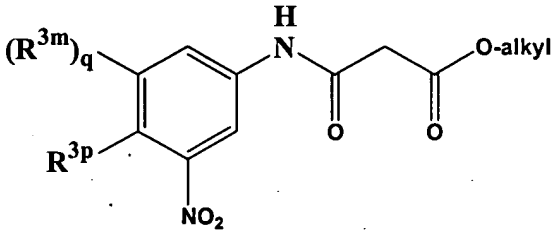


IIb

with an alkyl ester of malonic acid chloride:

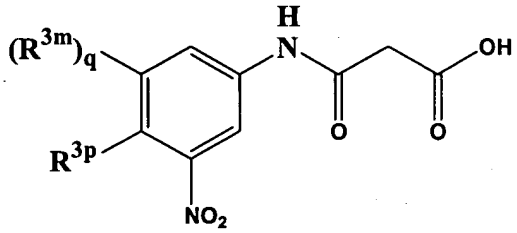


to yield a carboxylic ester compound of formula IIIb:



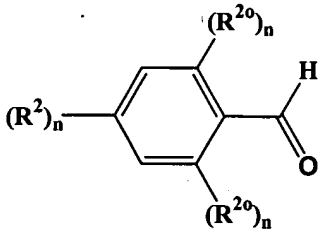
IIIb

(2) hydrolyzing the carboxylic ester compound of formula IIIb to form a carboxylic acid compound of formula IVb; and



IVb

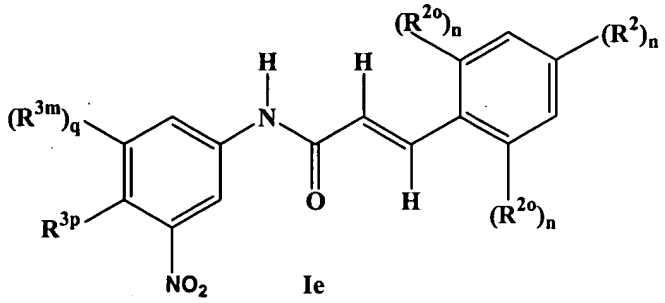
(3) coupling of the carboxylic acid compound of formula IVb with an aromatic aldehyde of formula V:



Vb

in glacial acetic acid at elevated temperature to form a compound of formula Ie;
or a salt of such a compound.

30. (withdrawn) A process for preparing a compound according to claim 16, which compound has the formula Ie:



Ie

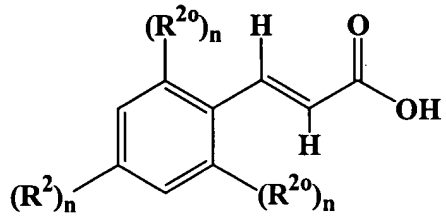
wherein:

q is 0 or 1; and

R^2, R^{2o}, R^{3m}, R^{3p} and n are defined as in claim 16;

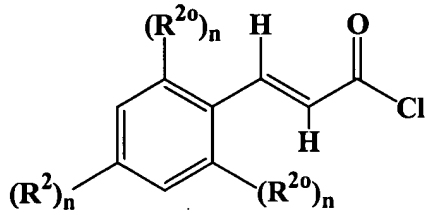
comprising:

(1) halogenating a carboxylic acid of formula VIb with a halogenating agent:



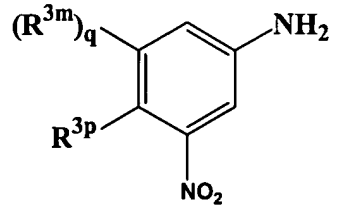
VIb

to form an acid halide of formula VIIb:



VIIb

(2) coupling the acid halide VIIb to an aromatic amino compound of formula IIb

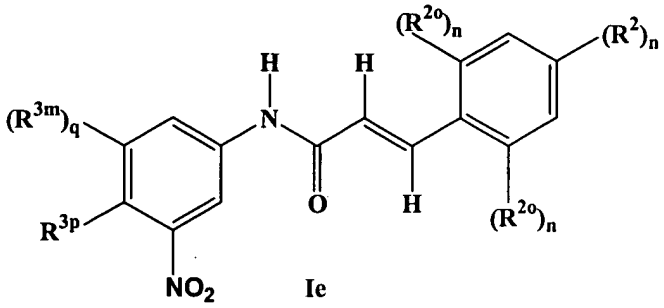


IIb

to form an amide compound of formula Ie;

or a salt of such a compound.

31. (withdrawn) A process for preparing a compound according to claim 16, which compound has the formula Ie:



Ie

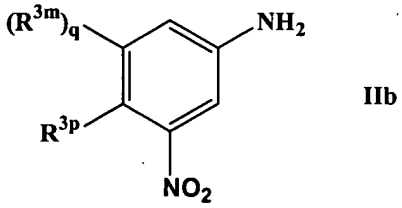
wherein:

q is 0 or 1; and

R^2, R^{2o}, R^{3m}, R^{3p} and n are defined as in claim 16;

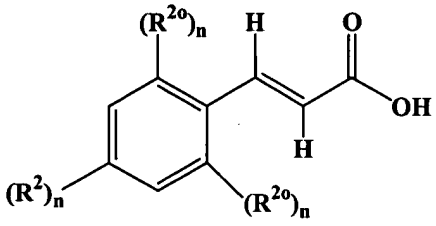
comprising:

(1) reacting an aromatic amino compound of formula IIb



IIb

with a carboxylic acid compound of formula VIb:



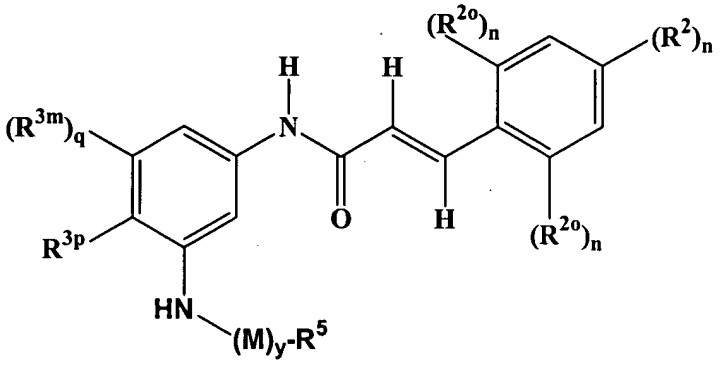
VIb

and an amide coupling agent,

to form a compound of formula Ie;

or a salt of such a compound.

32. (withdrawn) A process for preparing a compound according to claim 21, which compound has the formula Ic:



Ic

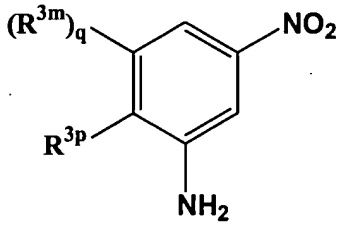
wherein:

q is 0 or 1; and

R^2, R^{2o}, R^{3m}, R^{3p}, n, M, y and R^5 are defined as in claim 21;

comprising:

(1) reacting an aromatic amine of formula IX



IX

with an electrophilic compound of formula VIII:

$$R^5—L \qquad \text{VIII}$$

wherein L comprises an electrophilic reactive center selected from the group consisting of:

(a) an alkyl moiety having a leaving group;

(b) an aryl or heteroaryl halide or aryl or heteroaryl pseudo halide;

(c) a carboxylic acid activated with a leaving group;

(d) a sulfonic acid activated with a leaving group;

(e) a carbamic acid moiety activated with a leaving group;

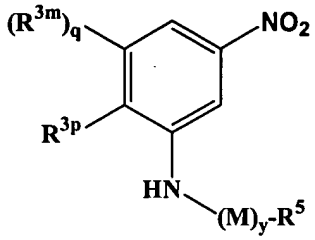
(f) a cyanate moiety;

(g) an aldehyde or ketone moiety, or a hydrate thereof or a ketal or acetal thereof;

(h) a carboxylic acid moiety and an amide coupling reagent; or

(i) the intermediate product of a thiourea moiety and 2-chloro-1-methyl pyridinium iodide;

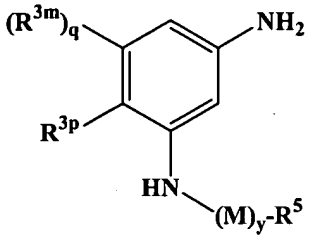
to form a compound of formula IXa:



IXa

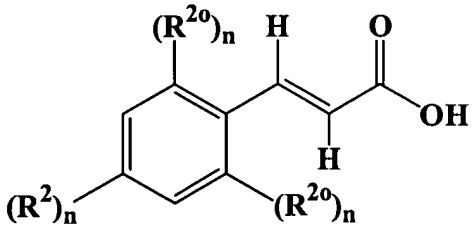
(2) optionally protecting the $-NH-(M)_y-R^5$ moiety in the formula IXa compound;

(3) chemically reducing said compound of formula IXa to form the aromatic amine IXb:



IXb

(4) reacting aromatic amine IXb with a carboxylic acid compound of formula VIb:



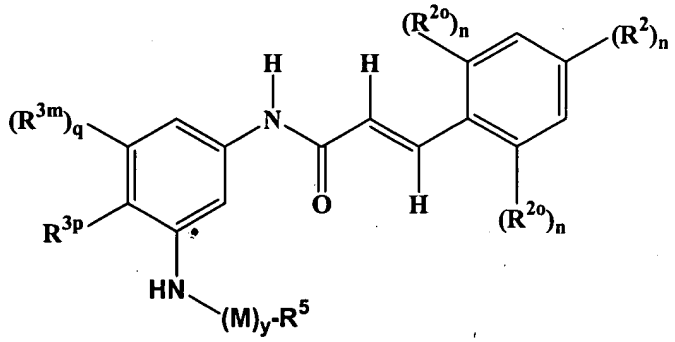
VIb

and an amide coupling agent; and

(5) optionally removing said protecting group to form a compound of formula Ic;

or a salt of such a compound.

33. (withdrawn) A process for preparing a compound according to claim 21, which compound has the formula Ic:



Ic

wherein:

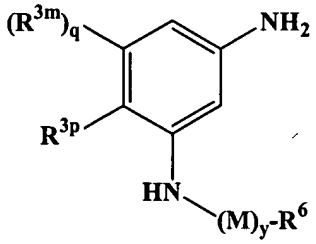
q is 0 or 1;

R^2, R^{2o}, R^{3m}, R^{3p}, n, M, y and R^5 are defined as in claim 21; and

the olefin double bond is in the *E* conformation;

comprising:

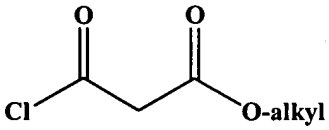
(1) coupling a compound of formula IXb:



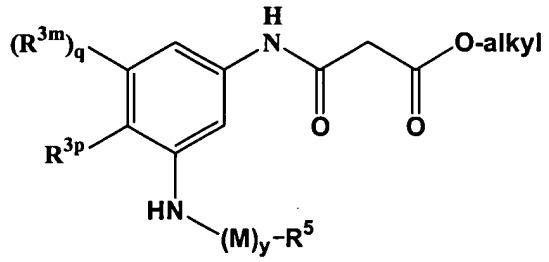
IXb

wherein the –NH-$(M)_y$-R^5 moiety is optionally protected with a protecting group;

with an alkyl ester of malonic acid chloride:

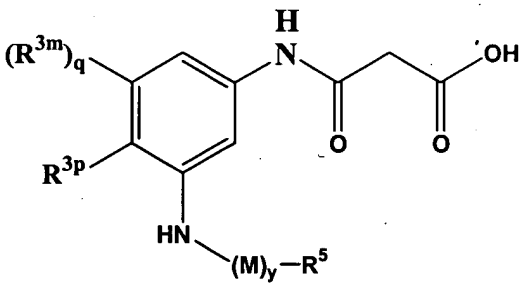


to yield a carboxylic ester compound of formula IXc:



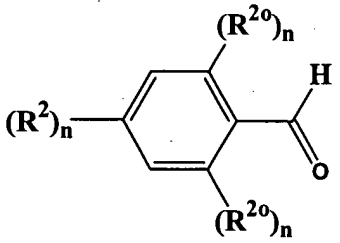
IXc

(2) hydrolyzing the carboxylic ester compound of formula IXc to form a carboxylic acid compound of formula IXd;



IXd

(3) coupling the carboxylic acid compound of formula IXd with an aromatic aldehyde of formula Vb:



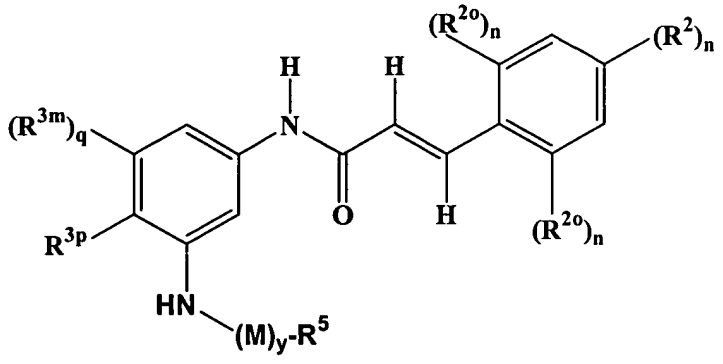
Vb

in glacial acetic acid at elevated temperature; and

(4) optionally removing said protecting group to form a compound of formula Ic;

or a salt of such a compound.

34. (withdrawn) A process for preparing a compound according to claim 21, which compound has the formula Ic:



Ic

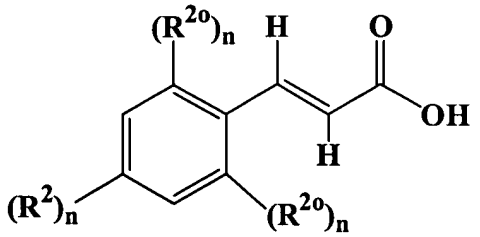
wherein:

q is 0 or 1; and

R^2, R^{2o}, R^{3m}, R^{3p}, n, M, y and R^5 are defined as in claim 21;

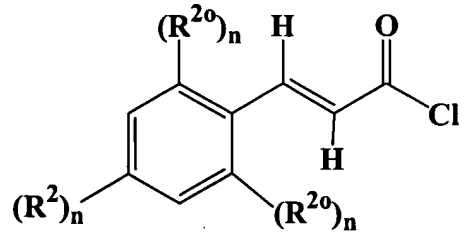
comprising:

(1) halogenating a carboxylic acid of formula VIb with a halogenating agent:



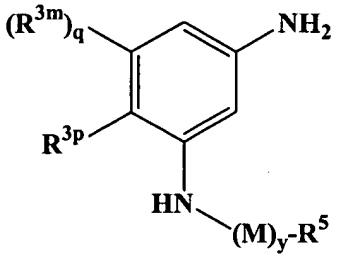
VIb

to form an acid halide of formula VIIb:



VIIb

(2) coupling the acid halide VIIb to an aromatic amino compound of formula IXb:



IXb

wherein the $-NH-(M)_y-R^5$ moiety is optionally protected with a protecting group; and

(3) optionally removing said protecting group to form an amide compound of formula Ic; or a salt of such a compound.

35. (original) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and at least one compound according to claim 1.

36. (cancelled)

37. (withdrawn) A conjugate of the formula, I–L–Ab;
wherein:

I is a compound according to claim 1;

Ab is an antibody; and

–L– is a single covalent bond or a linking group covalently linking said compound to said antibody.

38-41. (cancelled)

42. (withdrawn) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and at least one conjugate according to claim 37.

43. (currently amended) A method of treating an individual for a ~~proliferative disorder~~ cancer selected from breast cancer, prostate cancer, lung cancer and colorectal cancer comprising administering to said individual an effective amount of at least one compound ~~according to claim 1,~~ selected from the group consisting of: (*E*)-*N*-(4-methoxy-3-aminophenyl)-3-(3,4,5-trimethoxyphenyl)-2-propenamide;
(*E*)-*N*-(4-methoxy-3-nitrophenyl)-3-(2,3,4,5,6-pentafluorophenyl)-2-propenamide;

(*E*)-*N*-(4-bromophenyl)-3-(3-methoxy-4-fluorophenyl)-2-propenamide;
(*E*)-*N*-(4-bromophenyl)-3-(3-cyano-4-fluorophenyl)-2-propenamide;
(*E*)-*N*-(4-methoxy-3-aminophenyl)-3-(3-fluoro-4-aminophenyl)-2-propenamide;
(*E*)-*N*-(4-methoxyphenyl)-3-(2,4,6-trimethoxyphenyl)-2-propenamide;
(*E*)-*N*-(4-methoxyphenyl)-3-(2,6-dimethoxyphenyl)-2-propenamide;
(*E*)-*N*-(3-hydroxy-4-methoxyphenyl)-3-(2,4,6-trimethoxyphenyl)-2-propenamide;
(*E*)-*N*-(4-methoxy-3-aminophenyl)-3-(2,4,6-trimethoxyphenyl)-2-propenamide;
(2E)-*N*-[4-methoxy-3-(2,2,2-trifluoroacetylamino)phenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide; ~~or a salt~~ and salts thereof.

44-49. (cancelled)

50. (currently amended) A method of selectively inducing apoptosis of tumor cells selected from the group of tumors consisting of breast, prostate, lung, and colorectal tumors in an individual afflicted with cancer comprising administering to said individual an effective amount of at least one compound ~~according to claim 1,~~ selected from the group consisting of: (*E*)-*N*-(4-methoxy-3-aminophenyl)-3-(3,4,5-trimethoxyphenyl)-2-propenamide;
(*E*)-*N*-(4-methoxy-3-nitrophenyl)-3-(2,3,4,5,6-pentafluorophenyl)-2-propenamide;
(*E*)-*N*-(4-bromophenyl)-3-(3-methoxy-4-fluorophenyl)-2-propenamide;
(*E*)-*N*-(4-bromophenyl)-3-(3-cyano-4-fluorophenyl)-2-propenamide;
(*E*)-*N*-(4-methoxy-3-aminophenyl)-3-(3-fluoro-4-aminophenyl)-2-propenamide;
(*E*)-*N*-(4-methoxyphenyl)-3-(2,4,6-trimethoxyphenyl)-2-propenamide;
(*E*)-*N*-(4-methoxyphenyl)-3-(2,6-dimethoxyphenyl)-2-propenamide;
(*E*)-*N*-(3-hydroxy-4-methoxyphenyl)-3-(2,4,6-trimethoxyphenyl)-2-propenamide;
(*E*)-*N*-(4-methoxy-3-aminophenyl)-3-(2,4,6-trimethoxyphenyl)-2-propenamide;
(2E)-*N*-[4-methoxy-3-(2,2,2-trifluoroacetylamino)phenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide; ~~or a salt~~ and salts thereof.

51-52. (cancelled)

53. (withdrawn) A method of treating an individual afflicted with cancer, comprising administering to said individual an effective amount of at least one conjugate according to claim 37.

54-82. (cancelled)

83. (withdrawn - currently amended) A compound according to claim 21, wherein:

M is –(C_1-C_6)alkylene–;

y is 1;

R^4 is –H or -(C_1-C_6)alkyl;

R^5 is -CO_2R^4; and

[[Q]] q is 0; or a salt of such a compound.

84-89. (cancelled)

90. (previously presented) A compound according to claim 1 wherein a is 2 or 3.

91. (previously presented) A composition according to claim 35 wherein a is 2 or 3.

92. (new) A compound according to claim 8, wherein the compound is selected from the group consisting of: (*E*)-*N*-(4-methoxy-3-nitrophenyl)-3-(3,4,5-trimethoxyphenyl)-2-propenamide;

(*E*)-*N*-(4-methoxy-3-aminophenyl)-3-(3,4,5-trimethoxyphenyl)-2-propenamide;

(*E*)-*N*-(4-methoxy-3-nitrophenyl)-3-(2,3,4,5,6-pentafluorophenyl)-2-propenamide;

(*E*)-*N*-(4-methoxy-3-nitrophenyl)-3-(3-fluoro-4-nitrophenyl)-2-propenamide;

(*E*)-*N*-(4-methoxy-3-aminophenyl)-3-(3-fluoro-4-aminophenyl)-2-propenamide;

(*E*)-*N*-(4-methoxy-3-nitrophenyl)-3-(2,4,6-trimethoxyphenyl)-2-propenamide;
(*E*)-*N*-(4-methoxy-3-aminophenyl)-3-(2,4,6-trimethoxyphenyl)-2-propenamide;
(2E)-*N*-[4-methoxy-3-(2,2,2-trifluoroacetylamino)phenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide; and salts of such compounds.

93. (new) A compound according to claim 8, wherein the compound is (*E*)-*N*-(3-hydroxy-4-methoxyphenyl)-3-(2,4,6-trimethoxyphenyl)-2-propenamide, or a salt thereof.

94 (new) A compound according to claim 83, wherein the compound is selected from the group consisting of: 2-({5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}amino)acetic acid; 2-({5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}amino)propanoic acid; 4-({5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}amino)butanoic acid; 3-({5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}amino)propanoic acid; and salts of such compounds.